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10/070,161	03/04/2002	Yuichi Oku	MIT-C205	9188

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EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 03/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/070,161	OKU ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01/10/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *2,3,24 and 25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/20/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I claims 1, 4-6 and 8-23 in the reply filed on January 10, 2005 is acknowledged. The traversal is on the ground(s) that at least one special technical feature is common to the claims of all three groups. Specifically, each kit of Group I, II and III of the present invention comprises a receptor I capable of binding to an analyte; a receptor II having a bond element B3 capable of binding to an anti-bond element R3 and capable of binding to an analyte; and the anti-bond element R3 bound to a solid phase and the foregoing structure and features are common to the claims of Group I, II and III. This is not found persuasive because as stated in the previous office action there are three different kits and methods using different compounds and thus there are three different inventions and under Rule 13 Applicant is entitled to one product, a process for manufacture of the product and a use of said product. Therefore, lack of unity is maintained and the requirement is still deemed proper and is therefore made FINAL.

Note: after further consideration claim 7 has been included with claims 1, 4-6 and 8-23. Therefore, Group I consists of claims 1 and 4-23.

Information Disclosure Statement

The supplemental information disclosure statement filed August 1, 2002 pertaining to a translation of the "International Preliminary Examination Report" has been placed in the application. However, a 1449 form was not received and therefore the supplemental information disclosure statement as not been considered.

Specification

The disclosure is objected to because of the following informalities: The specification lists amino acids sequences which are greater than four amino acids. Specifically on page 21, line 21 – page 22, line. For example, the disclosure refers to Amino group – GAA TTC CCG GGG ATC CGT CG as "pair 1+". This is not considered normal U.S. practice concerning sequence listings in the specification. The amino acids should be referred to by SEQ ID No.s. Therefore the application does not meet sequence compliance rules.

Appropriate correction is required.

Claim Objections

2. Claims 21 and 22 are objected to because of the following informalities: Claims 21 and 22 depend from claims 1-3. Claims 2 and 3 are directed toward non-elected claims and therefore claims 21 and 22 should depend only from claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1 and 4-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite because it is unclear if the compound L1-B1-R1-M is an intact compound or if it is two separate compounds in the kit, which are later

combined together to form the compound. Claim 1 recites a compound L1-B1-R1-M comprising a compound R1-M bound to a compound L1-B1. The claim further recites that R1 is capable of binding to B1, which insinuates that the two are not actually bound together but are able to be bound together. Thus it is unclear if the compound L1-B1-R1-M is a single compound in the kit or if the kit comprises two separate compounds R1- M and L1-B1 which are later combined to form receptor I compound. Please clarify. See also deficiency found in claim 23.

Claim 1 is vague and indefinite because it is unclear if the compound L2-B2-R2-B3 is an intact compound or if it is two separate compounds in the kit, which are later combined to form the compound when using the kit. The claim recites a compound L2-B2 previously bound to a compound R2-B3. However, the claim later recites that substance R2 being capable of binding to the substance B2, which insinuates that the two are not actually bound together but are able to be bound together. Thus it is unclear if the compound L2-B2-R2-B3 is a single compound in the kit or if the kit comprises two separate compounds L2-B2 and R2-B3 which are later combined to form receptor I compound. Please clarify. See also deficiency found in claim 23.

Claim 1, line 17 the recitation "introduced into the ligand" is vague and indefinite. It is unclear what applicant intends. Does B2 bind to L2? Does L2 engulf B2? Do B2 and L2 merely come in contact with each other? Please clarify. See also deficiency found in claim 23.

Claim 1, lines 18-19 "the substance B2 having different binding capability from the analyte A" is vague and indefinite. It is unclear what applicant intends. Does

applicant intend that B2 binds to analyte A or does applicant intend something else? Please clarify. See also deficiency found in claim 23.

Claim 1, lines 22-23 the recitation "B3 having binding capability different from the substance B2" is vague and indefinite. It is unclear what applicant intends.

Claim 1, step (3) the recitation "anti-bond element" is vague and indefinite. It is unclear what applicant is referring to. In the art of assay the term "anti-" is interpreted as antibody. Is applicant referring to an antibody or something else such as DNA or chemical functional group? Please clarify.

Claim 4, line 3 "the medium" there is insufficient antecedent basis for this limitation. It is unclear what applicant is referring to. See also deficiency found in claim 23.

Claim 5 the recitation "plural types of reactivity" is vague and indefinite because it is unclear what types of reactivity applicant is referring to. See also deficiency found in claim 7. The disclosure on page 38 discloses that the plural ligands may have the same reactivity or may have plural types of reactivity.

Claim 6 the recitation "or ligands L3" is vague and indefinite. There is no recitation of L3 in claim 1.

Claim 6 the recitation "the medium" there is insufficient antecedent basis for this limitation.

Claim 7 the recitation "or ligands L3" is vague and indefinite. There is no recitation of L3 in claim 1. See also deficiency found in claim 10.

Claim 8 the recitation "at least independent of" is vague and indefinite. It is unclear what applicant intends.

Claim 12, the recitation "the ligand L3" there is insufficient antecedent basis for this limitation.

Claim 12 the recitation "having different sequences with one another" is vague and indefinite. It is unclear what applicant intends. The L1 and L2 ligands do not bind to each other in the assay therefore, it is confusing what applicant intends. Does applicant intend that the two ligands are different and bind to different epitopes of the antigen or does applicant intend that one is an analog of the other? Please clarify.

Claim 13, line 3 is vague and indefinite because it is unclear if the recitation M contained within the parenthesis () is actually part of the claim or not. Further, is the M in the parenthesis referring to the marker M of claim 1 or to something else.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: a separation or washing step to remove unbound materials following the formation of complexes and prior to the detection step. Because without this step to remove unbound marker, one would always obtain a positive signal no matter if binding occurred or not.

Claim 23, step (4) is vague and indefinite because it is unclear what complex applicant is referring to. In step three applicant recites that the substance R2 being capable of binding to the substance B2, the bond element B3 having binding capability different from the substance B2, to reach with one another to thereby from a complex.

Is applicant referring to the complex of R2-B2 or is applicant referring to the complex of receptor II with the analyte or is applicant referring to the complex of receptor I/analyte/receptor II. Please clarify.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1, 9-11, 13, 14, 16, 18, and 20-23 are rejected under 35 U.S.C. 102(e) as being anticipated by Niemeyer et al (US 2003/0118595).

Niemeyer et al disclose methods and bioconjugates for determining a target analyte of interest. Niemeyer et al disclose a solid phase (chip) having oligonucleotides (R3) immobilized on the solid phase (p. 14, paragraph 0127, lines 1-5). Niemeyer et al disclose a bioconjugate (receptor II) comprising DNA-STV hybrids (DNA (B3)- STV (strepavidin, R2) bound to a biotinylated (B2) antibody (L2) (p. 14, para. 0127, lines 9-10). Niemeyer et al disclose that the solid phase oligonucleotides (R3) is capable of binding to the DNA (B3) of the DNA-STV hybrid. Niemeyer et al disclose that the bioconjugate binds to a target analyte such as an antibody (p. 14, para. 0127, lines 11-13). Niemeyer et al disclose that the target can be detected by another conjugate (receptor I). Niemeyer et al disclose that this conjugated compound comprises

biotinylated (B1) antibody (L1) combined with streptavidin (R1) coupled to nucleic acid (M) (p. 8, para. 0079, lines 43-60). Niemeyer et al disclose that the bioconjugates can be packaged into a kit (p. 2, para. 0017). Niemeyer et al disclose that the solid phase can be comprised of cellulose (p. 4, para. 0044).

With respect to claim 13 since Niemeyer et al disclose the same substances B1, R1, B2 and R2 as applicant. It is inherent that the dissociation constant be from 10^{-8} to 10^{-16} (M).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 4- 8 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al (US 2003/0118595) in view of Bayer et al (Immunoassay, edited by Diamandis et al, Chapter 11, The Avidin-Biotin System, 1996, pgs 237-267).

See above for the teachings of Niemeyer et al.

Niemeyer et al differ from the instant inventions in failing to specifically teach the R1 or R2 has a plurality of binding points with respect to B1 or B2, and a plurality of ligands L1 or L2 are bound to the R substances by the medium of B substances.

Bayer et al disclose that avidin (R1 or R2 of Niemeyer) (interchangeable with strepavidin, p. 238) occurs in solution as a tetramer and thus has four binding biotin-binding sites per molecule (p.238). Niemeyer et al disclose that a plurality of biotinylated probes such as biotinylated (B1 or B2) antibodies (L1 or L2) can bound to avidin (R1 or R2) (pgs 251-252). Bayer et al disclose that this provides for the introduction of preformed complexes and that the signals achieved using complexes are often superior to those achieved using conjugates (p. 251-252).

It would have been obvious to incorporate a plurality of biotinylated antibodies such as taught by Bayer et al into the method and kit of Niemeyer et al because Niemeyer et al specifically teaches the use of avidin – biotin systems and Bayer et al teach these systems provide for the introduction of preformed complexes and that the

signals achieved using complexes are often superior to those achieved using conjugates

With respect to claims 5 and 7 as instantly recited since the combination of Niemeyer et al and Bayer et al disclose the same bioconjugates as recited in the claims the bioconjuates of Niemeyer et al and Bayer et al would appear to have plural types of reactivity. Further, Niemeyer et al disclose that the ligand can be a polyclonal antibody (p. 7) which binds to different epitopes on an antigen. Therefore, it appears that Niemeyer et al teaches the antibodies have plural types of reactions.

With respect to the recitation "wherein the solid phase conjugate is at least independent of the receptor II" as recited in claim 8. Niemeyer et al discloses the claimed invention except for the solid phase conjugate is at least independent of the receptor II. It would have been obvious to one having ordinary skill in the art at the time the invention was made to make the solid phase conjugate separate from receptor II, since it has been held that constructing a formerly integral structure in various elements involves only routine skill in the art. *Nerwin v. Erlichman,* 168 USPQ 177, 179.

With respect to claim 19 since Bayer et al teaches that avidin and streptavidin are interchangeable and are actually different molecules. It would have been obvious to one of ordinary skill in the art to replace one with the other in one of the receptor molecules because it is known in the art that avidin is an alternative for strepavidin and vice versa.

11. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al in view of Van Ness et al. (US 5,667,976).

See above for teachings of Niemeyer et al.

Niemeyer et al differ from the instant invention in failing to teach the ligands L1 and L2 are substances having different sequences with one another.

Van Ness et al disclose assays using a capture oligonucleotide which binds a target. Van Ness also discloses a labeled oligonucleotide which also binds the target to form a sandwich of the capture oligonucleotide probe:target nucleic acid:signal oligonucleotide probe.

It would have been obvious to one of ordinary skill in the art to substitute the oligonucleotide ligands as taught by Van Ness et al for the ligands of Niemeyer et al because Niemeyer et al disclose that nucleic acids can be used as binding partner for binding targets (p. 6 Niemeyer et al) and further because Niemeyer et al is generic with respect to the target to be detected and one of ordinary skill in the art would use the appropriate regents i.e. oligonucleotides to determine the target of interest in this case target nucleic acids.

12. Claims 15 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niemeyer et al in view of Billing-Medel et al (US 2002/0142371).

See above for teachings of Niemeyer et al.

Niemeyer et al differ from the instant invention in failing to specifically teach that the B1 and/ or the substance B2 and wherein the substance R1 and/or the substance R2 is selected from the group consisting of DNA, RNA, antigen, antibody, lectin, glycoprotein, and sugar.

Billing-Medel teach assays in which specific binding members are used. Billing Medel teaches that specific binding member is a member of a specific binding pair. That is two different molecules where one of the molecules, through chemical or physical means, specifically binds to the second molecule. Billing-Medel teaches that antigen and antibody specific binding pairs are common in immunoassays and that other specific binding pairs include biotin and avidin, and carbohydrates and lectins.

It would have been obvious to one of ordinary skill in the art to incorporate antigen/antibody pairs as taught by Billing-Medel et al into the method of Niemeyer et al because Billing-Medel et al teaches that the use of antigen/antibody pairs are known in the art. Therefore, one of ordinary skill in the art would have a reasonable expectation of success incorporating antigen/antibody pairs as taught by Billing-Medel et al into the method and kit of Niemeyer et al.

Conclusion

13. No claims are allowed.

14. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

LaMotte, III (US 5,296,347) teaches the combination of multiple binding pairs to form receptors.

Carney (US 6,200,764) teaches a detection molecule comprising biotinylated antibody bound to avidin-horse radish peroxidase.

Goldberg et al. (US 6,203,989) disclose complexes comprising labeled streptavidin and biotinylated antibody.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
March 10, 2005

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